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Date: October 22, 2014, (**3 pages - replaces version dated October 16, 2014**)

To: All North Carolina Health Care Providers
From: Megan Davies, MD, State Epidemiologist
RE: **Respiratory Infections due to Enterovirus D68 (EV-D68)**

Since mid-August, 2014, enterovirus D68 (EV-D68) has been increasingly identified in association with respiratory illness outbreaks across the country. The first cases of EV-D68 infection in North Carolina were confirmed on September 22, 2014. This memo is intended to provide general information regarding EV-D68 and recommendations for North Carolina health care providers.

This version has been updated to include additional information about acute neurologic illness possibly associated with EV-D68; instructions for reporting of similar illnesses; and a link to North Carolina surveillance updates.

Enteroviruses – Background

Enteroviruses are very common viruses. There are more than 100 types of enteroviruses. It is estimated that 10–15 million enterovirus infections occur in the United States each year. Most people infected with enteroviruses have no symptoms or only mild symptoms, but some infections can be serious. Most enterovirus infections in the United States occur seasonally during the summer and fall, and outbreaks tend to occur in several-year cycles.

Clinical and Epidemiologic Features

EV-D68 is an enterovirus that was first isolated in California in 1962 and has been reported infrequently since that time. EV-D68 has been associated almost exclusively with respiratory disease, which can range from mild to severe. The full clinical spectrum of EV-D68 illness is not well-defined.

EV-D68 has been identified with increasing frequency during recent years, sometimes in association with large respiratory illness clusters in the United States and elsewhere. Whether this increase in recognized cases is attributable to improved diagnostics or emergence of the pathogen is unknown. EV-D68 infections appear to be more common in the fall. No data are available regarding the overall burden of morbidity or mortality from EV-D68 in North Carolina or elsewhere in the United States.

Acute Neurologic Illness with Focal Limb Weakness

On September 26, 2014, the Centers for Disease Control and Prevention (CDC) issued a Health Advisory describing a cluster of nine pediatric patients hospitalized with acute neurologic illness of undetermined etiology. The illness was characterized by focal limb weakness and abnormalities of the spinal cord gray matter on MRI. EV-D68 was associated with some, but not all, of these cases. The CDC issued a request to all states to report similar neurologic illnesses. National investigation updates are posted weekly at www.cdc.gov/ncird/investigation/viral/sep2014.html.

www.ncdhhs.gov • <http://epi.publichealth.nc.gov/cd/>
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To be considered a case, patient must meet ALL 4 of the following:

1. Patient is less than 21 years of age,
2. Acute onset of focal limb weakness,
3. On or after August 1, 2014 AND
4. An MRI showing a spinal cord lesion largely restricted to gray matter.

Diagnosis

Enteroviruses can be detected by several commercial, multi-pathogen detection systems. However, the sensitivity of these systems for EV-D68 detection is unknown. Some of these systems use broadly reactive primers that amplify RNA from either human rhinoviruses or enteroviruses, and results are reported as "entero-rhinovirus" or "human rhinovirus/enterovirus". Most hospital and commercial laboratories are not able to perform enterovirus typing.

The North Carolina State Laboratory of Public Health (NCSLPH) offers viral culture to detect rhinoviruses and enteroviruses and serotyping for the detection of several specific enteroviruses, including enterovirus 70 and 71, echoviruses and coxsackieviruses.

The gold standard test for EV-D68 identification is "real-time" reverse transcription polymerase chain reaction, or rRT-PCR. Facilities or providers interested in the specific detection of EV-D68 can submit specimens to the NCSLPH for submission to the CDC. Testing prioritization will be based on severity of illness. **Providers should contact their local health department or the Communicable Disease Branch epidemiologist on-call (919-733-3419) prior to submitting specimens.**

Acceptable specimen types for patients with respiratory illness include nasopharyngeal (NP) or oropharyngeal (OP) swabs in viral transport media (> 1ml) or an NP/OP wash or aspirate (> 1ml). Specimens should be collected within 1 week of illness onset, preferably within 48 hours post-onset. Specimens should be shipped on cold packs or dry ice. Please contact Myra Brinson (919-807-8835) or Peggy Brantley (919-807-8820) at the NCSLPH if you have questions regarding enterovirus testing and specimen collection and shipment.

All specimen submissions must be accompanied by the following:

1. A completed CDC 50.34 DASH form (<http://slph.state.nc.us/Forms/CDC-Dash-NCSLPH-013114.pdf>);
2. A completed NCSLPH virology form (<http://slph.state.nc.us/Forms/DHHS-3431-Virology-20130809.pdf>); and
3. A completed CDC patient summary form (http://www.cdc.gov/non-polio-enterovirus/downloads/EV68_PatientSummaryForm.doc).

For patients with acute neurologic illness with focal limb weakness of unknown etiology, the requested specimens include cerebrospinal fluid, upper respiratory tract specimen, serum samples, and two stool specimens. For further details please see: <http://www.cdc.gov/ncird/investigation/viral/specimen-collection.html>. In addition to the forms listed above, providers must complete and submit a patient summary form specific to this investigation, available at: <http://www.cdc.gov/ncird/downloads/patient-summary-form.docx>.

- **NOTE: The CDC patient summary form(s) should first be faxed to the Communicable Disease Branch at 919-733-0490 (attention: Anita Valiani) and then included with the specimen for submission.**

Treatment

There is no specific treatment for EV-D68 infections. Many infections will be mild and self-limited, requiring only symptomatic treatment. Patients with asthma exacerbations or other more severe manifestations may require hospitalization for supportive therapy. Vaccines for preventing EV-D68 infections are not currently available.

Since patients with asthma are at risk for more severe illness, providers should ensure that these patients have an asthma action plan. Reinforce use of this plan, including adherence to prescribed long-term control medication. Encourage people with asthma who are experiencing an exacerbation to seek care early.

Public Health Recommendations

To help reduce the risk of infection with EV-D68 and other respiratory viruses, health care providers should recommend the following:

1. Wash hands often with soap and water for 20 seconds;
2. Avoid touching eyes, nose, and mouth with unwashed hands;
3. Avoid kissing, hugging, and sharing cups or eating utensils with people who are sick;
4. Disinfect frequently touched surfaces, such as toys and doorknobs, especially if someone is sick; and
5. Stay home when sick.

Infection Prevention

Contact and Droplet isolation precautions are recommended for patients in whom infection with EV-D68 or another respiratory virus is suspected. Some evidence suggests that alcohol-based hand rubs have limited activity against EV-D68 and other enteroviruses. Health care facilities should consider this information when determining whether to modify their hand hygiene policies.

As EV-D68 is a non-enveloped virus, environmental disinfection of surfaces in healthcare settings should be performed using a hospital-grade disinfectant with an EPA label claim for any of several non-enveloped viruses (e.g. norovirus, poliovirus, rhinovirus).

Reporting

Providers should be aware of EV-D68 as one of many causes of respiratory illness. Providers who identify clusters of severe or unusual respiratory illness are asked to contact their local health department or the Communicable Disease Branch epidemiologist on-call 24/7 number (919-733-3419).

Providers are also asked to notify local or state public health if they are aware of any patient ≤ 21 years of age who meets the following criteria:

1. Acute onset of focal limb weakness occurring on or after August 1, 2014;
- AND
2. An MRI showing a spinal cord lesion largely restricted to gray matter.

Additional information is available for providers and the public is available at <http://epi.publichealth.nc.gov/cd/diseases/enterovirus.html> and www.cdc.gov/non-polio-enterovirus/about/EV-D68.html. A map of EV-D68-positive lab results by region and additional surveillance information is available at <http://ncdhhs.gov/evd68/>. This is an evolving situation and recommendations may change as new information becomes available.

References

1. CDC (2014). Severe Respiratory Illness Associated with Enterovirus D68 — Missouri and Illinois, 2014. MMWR Morb Mortal Wkly Rep 63 – early release. Available at <http://www.cdc.gov/mmwr/pdf/wk/mm63e0908.pdf>. Accessed September 8, 2014.
2. CDC (2011). Clusters of acute respiratory illness associated with human enterovirus 68 – Asia, Europe, and United States, 2008–2010. MMWR Morb Mortal Wkly Rep 60, 1301–1304. Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6038a1.htm>. Accessed September 8, 2014.
3. CDC (2014). Health Advisory: Acute Neurologic Illness with Focal Limb Weakness of Unknown Etiology in Children Available at <http://emergency.cdc.gov/han/han00370.asp>.